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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,551	01/31/2002	Michael A. Apicella	875.045US1	2735

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,551	APICELLA ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,15,21 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7* is/are allowed.

6)☒ Claim(s) *1, 15,21 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's request for continued examination filed on 3/4/05 has been entered.

Amendment

2. The amendment filed on 8/9/04 is acknowledged.

Status of Claims

3. Claims 1, 7, 15 have been amended.

Claims 2-6, 8-14, 16-20, 22 and 26-59 are cancelled.

Claims 1, 7, 15, 21, 23-25 are under examination.

Information Disclosure Statement

4. Information Disclosure Statements filed on 8/9/04 and 3/4/05 are acknowledged. The examiner has reviewed the IDS filed on 8/9/04 and a signed copy is attached to this Office action. However, the IDS filed on 3/4/05 is the duplicate of 8/9/04 and therefore, it is not considered and marked as duplicate of 8/9/04.

Claim rejection 101 withdrawn

5. In view of amendment to claims 1 and 7, the rejection under 35 U.S.C. 101 is withdrawn.

Claim Rejections - 35 USC 112, first and second paragraph withdrawn

6. In view of amendment to the claims, the rejections under 35 USC 112, first and second paragraph are withdrawn.

Claim Rejections - 35 USC 102 withdrawn

7. In view of amendment to the claims, the rejection under 35 U.S.C. 102(a) as being anticipated by Parkhill 2000, Accession Number B81859 is withdrawn.

Claim Rejections - 35 USC 102 Maintained

8. Claims 1, 15, 21 under 35 U.S.C. 102(b) as being anticipated by Fraser et al 1999 WO9957280, Accession Number AAY 75751 is maintained as set forth in the previous office action.

Fraser et al disclose a novel polypeptide, SEQ.ID.NO: 2974. (See the attached sequence alignment and abstract) comprising 508 amino acids from *N.gonorrhoeae*. The art on pages 1396 and 1397 disclose the DNA and encoding protein. The art also discloses that protein is expressed by cloning the ORFs into expression vector. The polypeptide could be used as vaccine, immunogenic composition or to raise antibodies (see abstract) The antigen to which an immune response has to be elicited is in general in hydrophilic phase, buffer or saline and is routinely used in the art. Characteristic such as p55 is considered as the inherent property of the disclosed polypeptide that is encoded by nucleic acid because the disclosed polypeptide comprises 508 amino acids and is approximately 55 kD as molecular weight of each amino acid is approximately 110 daltons.

It is acknowledged that weight is given to every term in claims 1, 15 and 21. This is why the instant claims drawn to vaccine are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the immunogenic composition i.e., vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. However, under prior art rejections, the term vaccine is considered as a composition comprising an isolated polypeptide. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed on 8/9/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that Fraser et al's reference does not disclose all of the features of the amended claims 1, 7 and 15. At no point does the Fraser et al's reference disclose an isolation or purification of a polypeptide having the claimed amino acid sequence. Further, Fraser et al do

not disclose the molecular weight of the polypeptide as determined using SDS-PAGE or any other method. As such, the Fraser et al's reference provides only an amino acid sequence encoded by an *N. gonorrhoeae* open reading frame and does not anticipate the present claims.

The examiner would like to bring applicant's attention to examiner's rejection, as claim 7 is not rejected under Fraser et al. The examiner disagrees with the applicant with respect to claim 1 and 15 (a) because the prior art WO9957280 discloses isolated and purified (see pages 59-66) recombinant protein by cloning ORF into expression vector (see page 59-60, pages 1396 and 1397) and the disclosed polypeptide appears to be same as the claimed protein comprising a 55 kD polypeptide because the molecular weight of disclosed polypeptide having 508 amino acids is approximately 55 kD as molecular weight of each amino acid is approximately 110 daltons. Therefore, the prior art protein appears to be the same and therefore, this rejection is maintained.

New Claim Rejections based on Amendment

Claim rejection 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claim 15 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 15 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The product, polypeptide as claimed, has the same characteristics as that found in nature (i.e., infected individual contain bacterial polypeptides). To overcome this rejection the Examiner suggests the amendment of the claims to include purity limitations, which would distinguish the characteristics of applicant's product from the product, as it exists in nature. It is further suggested that such limitation include the terminology " purified and

isolated" (i.e. if such purity is supported in the specification) and/or a description of what applicant's protein is "free of" relative to the natural source. (see Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 Fed. 887, 890 (N.D. Ill. 1909) (text of claim at 889); Parke-Davis & Co. v. H.D. Mulford Co., 189 Fed. 95, 103, 106, 965 (S.D.N.Y. 1911) (claim 1); and In re Bergstrom, 427 F.2d 1394, 1398, 1401-1402 (CCPA 1970).

Claim rejection 35 USC 112, first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 15, 21 and 23-25 (vaccine composition) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims are evaluated for enablement using the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is drawn to a vaccine composition for the treatment or cure of a disease or prevention of an infection caused by *Neisseria gonorrhea.* The state of the art indicates (Barritt et al, Infect and Immu1987, 55:2026-2031) the outermembrane protein antigens of *N.gonorrhoeae* are highly variable. The family of proteins that show variation are

the surface exposed proteins II (P II) and Opa proteins. These variations enable the bacterium to evade the host immune response and adapt to differing host environment.

Both pilin and Opa proteins undergo considerable variation in vivo as inoculation of strains FA1090 and strain MS11 with Opa negative population of gonococci resulted in reisolation of mostly Opa positive gononcocci indicating that there is a strong selection for expressing Opa proteins in vivo (see IDS,8/9/04 Cohen and Canon, JID 1999, 179(suppl) S375 –379). However, experimental studies are only pursued in men, since the complications in women would outweigh any potential benefits. The specification on pages 68- 78 recite that the antibodies to CR3, CD18 inhibit the binding of Neisseria to cervical epithelial cells. However, as claimed either the protein P55 or protein comprising the amino acid sequence SEQ.ID.NO: 4 (strains, MS11 and strain 1291, encoding secretion system) would directly inhibit the infectivity has not been shown. It is unpredictable whether the claimed composition induces an immune response sufficient to inhibit gonorrhea disease caused by various clinical strains of *Neisseria gonorrhea* because the prior art discloses that the human pathogen *N.gonorrhoeae* is endowed with a wide range of mechanisms that facilitate immune avoidance including antigenic shift in the expression of surface antigens. Because of this antigenic shift the development an effective vaccine has resulted in frustrated attempts (see introduction of Paz et al 1995, Microbiology 141, 913-920, reference cited in Form 892 7/20/03). The specification has not disclosed a link or nexus between the generation of protective immunity and the claimed polypeptide. Further, it is not routine in the art to use the claimed compositions for this purpose. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

Applicants' arguments filed on 8/9/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that the Examiner maintained the rejection of claims 15 and 21 under 35 U.S.C. 112, first paragraph, because it did not address the issue of whether a vaccine containing the claimed polypeptide would block invasion of *N. gonorrhoeae in vivo*. It is well established that there is no art-accepted animal model for human gonococcal infection, even though researchers have attempted to generate an effective animal model for the disease. See, for example, the Cohen and Cannon reference CJ Infect. Dis. (1999) 179(Supp1. 2): 5375-5379; copy attached), which teaches that there is no valid experimental animal model that might be useful to develop a gonorrhea vaccine. This reference also discloses that experimental gonorrhea cannot be pursued in women due to the likelihood of complications. Since experimental gonorrhea cannot be studied in women, primary cervical cells are an art-accepted system in which to evaluate the potential immunogenic use of *N. gonorrhoeae* proteins. Primary cervical cells are an established ex vivo model system for evaluating gonococcal infection, and have been used to generate data that is sufficient to support the present claims. In fact in the application and in the Declaration under 37 C.F.R. 1.132 that was filed with the response to the previous Office Action, Applicants used primary human cervical cells to show that the p55 protein of *N gonorrhoeae* is involved in modification of the cell membrane to enhance entry of the gonococcus. These experiments also established that p55 can be used to raise antibodies and thus provide protective immunity by interfering with gonococcal infection.

The examiner understands that that there are no practical experimental models that are suitable for studying the pathogenesis in women. The examiner again has carefully gone through the Declaration by professor Michael Apicella and understands that the antibody to PLD (phospholipase D/p55 kD), 1307 has the ability to block the infection of cervical cells

(endocervical or ectocervical cells) by blocking the access of *N. gonorrhoeae* to the CR3receptor on the surface of the cell (specification at page 48, lines 26 to page 49, line 2). However, the declaration provided by professor Michael Apicella and applicant's arguments have not addressed the issue whether the claimed isolated and purified 55kD protein from *N gonorrhoeae* or isolated and purified polypeptide comprising the amino acid sequence as set forth in SEQ.ID.NO: 4 would effectively prevent, ameliorate, or reduce the incidence of all *N gonhorrhoeae* strains in established ex vivo model system. At present the Declaration provides supporting evidence for a composition for treating women infected with *N. gonorrhoeae* comprising an immunogenic amount of an anti-phospholipase D (PLD) antibody 1307 that specifically binds to the peptide "RRMHNLSFTADNR " SEQ.ID.NO: 4.

Remarks

13. Claim 7 appears to be free of prior art and is allowed.

Claims 1, 15, 21 and 23-25 stand rejected.

14. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

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